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APPLICATION NUMBER: *60/392,468*
FILING DATE: *June 27, 2002*
RELATED PCT APPLICATION NUMBER: *PCT/US03/20430*

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This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53 (c).

INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Alan	Hargens	San Diego, CA
Kunihiko	Tanaka	San Diego, CA

☒ Additional inventors are being named on the 1 separately numbered sheets attached hereto

TITLE OF THE INVENTION (280 characters max)

METHOD AND DEVICE TO ENHANCE SKIN BLOOD FLOW

CORRESPONDENCE ADDRESS

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☒ Specification *Number of Pages* 24 ☐ CD(s), Number [ ]

☒ Drawing(s) *Number of Sheets* 17 ☐ Other (specify) [ ]

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

☒ Applicant claims small entity status. See 37 CFR 1.27.

☒ A check or money order is enclosed to cover the filing fees

FILING FEE AMOUNT ($) 80

☒ The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 11-0855

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☒ Yes, the name of the U.S. Government agency and the Government contract number are: NAG9-1916.

Respectfully submitted,

SIGNATURE Eleanor M. Musick Date 6/27/02

TYPED or PRINTED NAME Eleanor M. Musick REGISTRATION NO. *(if appropriate)* 35,623

TELEPHONE 404.541 6681 Docket Number: 51293/275447

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INVENTOR(S)/APPLICANT(S)

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James	Waldie	San Diego, CA

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TOTAL AMOUNT OF PAYMENT ($) 80

Complete if Known	
Application Number	
Filing Date	June 26, 2002
First Named Inventor	Hargens et al
Examiner Name	Unknown
Group / Art Unit	Unknown
Attorney Docket No	51293/275447

METHOD OF PAYMENT (check all that apply)

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101	740	201	370	Utility filing fee	
106	330	206	165	Design filing fee	
107	510	207	255	Plant filing fee	
108	740	208	370	Reissue filing fee	
114	160	214	80	Provisional filing fee	80

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Total Claims		- ** =	0	X		=	0
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Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claim, if not paid
109	84	209	42	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

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105	130	205	65	Surcharge - late filing fee or oath	
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139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	400	216	200	Extension for reply within second month	
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118	1,440	218	720	Extension for reply within fourth month	
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119	320	219	160	Notice of Appeal	
120	320	220	160	Filing a brief in support of an appeal	
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138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive – unavoidable	
141	1,280	241	640	Petition to revive – unintentional	
142	1,280	242	640	Utility issue fee (or reissue)	
143	460	243	230	Design issue fee	
144	620	244	310	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1 17 (q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	740	246	370	Filing a submission after final rejection (37 CFR § 1 129(a))	
149	740	249	370	For each additional invention to be examined (37 CFR § 1 129(b))	
179	740	279	370	Request for Continued Examination (RCE)	
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SUBMITTED BY

Name (Print/Type)	Eleanor M. Musick	Registration No. Attorney/Agent)	35,623	Complete (if applicable) Telephone	404 541.6682
Signature				Date	June 27, 2002

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METHOD AND DEVICE TO ENHANCE SKIN BLOOD FLOW

The invention comprises of a method and device to enhance skin microvascular circulation. The device is a hypobaric chamber fitted with a new non-occlusive seal and a vacuum pump. The seal is adjustable with minimal touch to the skin of the subject. The method involves placing a small body part inside the chamber and reducing the ambient pressure of the enclosed body part. Blood is sucked into the body part, but the treated area is so small that the shift does not unload carotid or cardiopulmonary baroceptors, and does not evoke reflexive vasoconstriction. Our new seal does not compress drainage veins, so it does not inhibit venous return. These effects result in a significant and stable increase in skin microvascular flow of the enclosed body part.

All previous pressure changing techniques to enhance circulation have differed from this invention in two ways. First, all previous techniques have relied on chambers with powerful airtight and skintight seal to make a pressure differential between the normal ambient pressure and pressure inside the chamber. These techniques cause occlusion of skin, blood vessels and their flow. Our device employs a loose non-occlusive seal that does not compress the skin.

Second, previous techniques involve a positive and negative pressure cycle. The cycle is commonly regulated according to cardiac rhythm, thereby amplifying the pump effect at the treated body part. The cyclical technique does not produce a stable increase in flow. Previous techniques actually produce a decrease or, at most, a minor

increase in blood flow, but our invention can increase skin blood flow by up to 90 times depending on the body part.

A hypobaric chamber can increase local blood flow by inducing a suction effect in the local artery, and by distending the capillaries and blood vessels to allow for the greater mass-flow rate. Past pressure chambers have employed airtight seals which occlude blood flow to and from the treated body part; our chamber utilizes a new seal which does not compress the skin. The seal is adjustable so that a small gap exists between the skin and the edge of the seal. The leak is overcome by a high-volume pump. Our chamber therefore provides for an unrestricted flow-through system, resulting in a continuous and very high local microcirculatory flow.

The invention is at the working prototype and experimental data stages. We have one working chamber, and another second generation chamber almost completed (please see photos attached). The chambers utilize various prototypes of seals. We have results for six subjects at various testing protocols (please see data attached). We adjusted the chamber pressure to 10 and 20mmHg below ambient pressure and obtained a very high and stable increase in skin blood flow. We have compared our new device with the effects of a tight seal in the same human subjects.

This hypobaric technique is pertinent to any ailment which would benefit from increased blood flow (and therefore oxygen and nutrient supply) and metabolites removal to and from a local body part. One prime focus is for the treatment of poor circulation like diabetic or atherosclerotic ulcers in the extremities, particularly the lower extremities. Surgical revascularizastion sometimes cannot be performed for

these patients. Some conservative treatment, i.e., dressings and other wound-care products are only adjuncts to careful local treatment, including pressure reduction for foot (a crutch, wheelchair, a walker), wound debridement, and infection control. Use of vasodilator drugs has not been found to aid healing in diabetic foot ulcers. Hyperbaric oxygen sometimes can be effective, but raising the oxygen content of the blood is of little value when the blood supply to the foot is severely impaired. Our method may treat such patients because of the significant increase in blood flow produced by our device. Our invention may also be a potential treatment for assisting the healing of wounds and burns.

Hypobaric chambers have been designed by other inventors for the scalp in an effort to alleviate baldness. These chambers have failed due to their occlusive effect. Our device is perceived to be more effective due to the non-occlusive seal we have designed.

ABSTRACT

Introduction: Current space suits are rigid, gas-pressurized shells that protect the astronauts from the vacuum of space. A tight elastic garment or in other words, mechanical counter pressure (MCP) suit that generates pressure by compression, may have several advantages over current space suit technology. In this study, we investigated local microcirculatory effects produced with and without a prototype of the MCP glove.

Methods: The right hand of 8 normal volunteers was subjected at normal ambient pressure, -50, -100, -150 mmHg below ambient pressure with and without the MCP glove. The pressure against the hand, skin microvascular flow and temperature at the dorsum of the hand, and middle finger girth were measured.

Results: The MCP glove generated approximately 200 mmHg at the skin surface. Without the MCP glove, skin microvascular flow and finger girth significantly increased with negative pressure, and the skin temperature decreased compared to the control condition. However, these changes were not observed with the MCP glove.

Discussion: The MCP glove generated pressure similar to the current gas-pressurized space suit gloves. The pressure at the skin surface remained constant during negative pressure due to unchanged elastic compression of the material. Skin microvascular flow and finger girth was increased with negative pressure, probably due to a blood shift toward the hand. Skin temperature might be decreased by enhanced heat transfer because of air inflow from a non-occlusive seal. However, the

MCP glove effectively maintained baseline values of the measured physiologic parameters despite exposure of the hand to various negative pressures.

Conclusions: The MCP glove generated effective counter pressure and countered the adverse effects of negative environmental pressure.

Key Words: extravehicular activity suit, mechanical counter pressure, microvascular flow, negative pressure

During extravehicular activity (EVA), current U.S. space suits are pressurized by gas with 100% oxygen at approximately 222 mmHg (1). Gas must be delivered to the lungs at a pressure sufficient to ensure diffusion of oxygen into the blood. The minimal design value is 150mmHg, 170mmHg is safer, and 200mmHg is quite conservative when pure oxygen is breathed in a vacuum by an active man with the suit (18). In addition, there must be volume compensating oxygen gas counter pressure applied to the chest and abdomen in order to match the alternating volume changes of respiratory movement (18). However, fire hazards are increased with pure oxygen. A higher pressure suit might be able to use a mixture of oxygen and nitrogen, and eliminate the risk of decompression sickness (8), but suit flexibility would be sacrificed.

As an alternate approach to improve the current EVA suit, mechanical counterpressure (MCP) is applied over the arms, legs and torso by a powerful elastic leotard to counteract adverse responses of the body to the vacuum of space. Moreover, MCP is designed to balance breathing pressure while oxygen is delivered to a closed helmet at 222 mmHg. . There are many potential advantages of an MCP suit (mobility, weight, simplicity) over the conventional space suit because no hard joints or bearings are needed (2, 17, 18). However, if a MCP suit generates too little pressure, decompression sickness results due to undissolved gas in the blood and tissues (16). If too much pressure is generated, cessation of blood flow, ischemic/compressive neuropathy, and compartment syndrome may occur, which may risk tissue viability (6). As the first step to develop the MCP suit, we chose a

small area but complex shape, which can simulate the other part of the body, i.e., the hand, that has cylindrical, flat and concave shapes. In the present study, we evaluated the physiological effects, especially, local microcirculatory effects produced by negative pressure exposures, with and without our prototype MCP glove.

MATERIALS AND METHODS

The right hands of 8 healthy male subjects, aged 22-34 years, were used. For recruiting subjects, we excluded volunteers who smoked or who had any past history of systemic disease or injury or surgery to their right hand. This study was approved by the Institutional Review Boards at the University of California, San Diego and NASA Johnson Space Center, and informed consent was obtained from all participating subjects.

A prototype MCP glove was developed by Honeywell, in collaboration with Webb Associates and Clemson University. The MCP glove assembly consisted of seven primary components: a comfort layer, a slip layer, an elastomeric layer, an inflatable layer, a gauntlet, a wrist seal bladder, and a wrist seal cuff. Each component had a specific design requirement and must function compatibly with the other components. The MCP glove assembly was connected to the current extravehicular mobility unit (EMU) lower arm assembly. The comfort layer was designed to cushion the hand from localized stresses and to begin to apply the MCP. The comfort layer consisted of a seamlessly knit glove (one piece with no seams) formed from plies of a flat nylon yarn and a low-power elastomeric yarn. The slip layer was designed to facilitate the

easy donning and doffing of the power layer. It consisted of a low-friction polytetrafluoroethylene (PTFE) yarn seamlessly knit into a glove. The power layer was designed to generate the required MCP on the hand. It was also a seamlessly knit glove formed from a high-power, high-elongation, elastomeric yarn. An inflatable layer was designed to provide mechanical counter pressure to flat portions of the hand. The gauntlet was designed to confine the inflatable layer, directing the mechanical counter pressure to appropriate portions of the hand. It was formed from a woven, high-modulus fabric that is shaped through the use of seams and pleats.

The wrist seal cuff serves as the interface between the MCP glove assembly and the EMU lower arm assembly. The cuff is integrated into the wrist side disconnect from a current EMU glove. For sealing and comfort on the forearm skin, a silicone-filled wrist seal bladder was inserted between the forearm and the wrist seal cuff. To avoid compression against the skin, and the cephalic vein at the wrist, an anti-compressive bridge was placed between the wrist and the seal.

To measure and record the pressure exerted on the hand, an Iscan system (Tekscan, South Boston, MA) was used with the 4300 vascular sensor array. The force sensing array was connected to an interface module and an A-D converter. The digitized signal of the compression force was sent to a computer and was recorded in real time. Prior to measurement, calibration was performed for the relation between the force and the pressure over a range of zero to 230 mmHg. The array was placed between the glove and the hand along the palm, the middle finger, and the dorsum of the hand (Figure 1).

[Figure 1 Here]

The averaged value of 20 seconds at each site was used for data of each condition.

A 2.5mm thick laser Doppler probe was placed at the dorsum of the hand and connected to a laser Doppler flowmeter (LASERFLO BPM403A, VASAMEDICS, St. Paul, MN) to measure skin blood flow. Skin temperature was recorded by a YSI 400 series thermistor placed near the laser Doppler probe. Volume changes of the middle finger were recorded with a mercury strain gauge plethysmograph (EC6 plethysmograph, Hokanson, Bellevue, WA). Arterial blood pressure and pulse rate were measured continuously at the left middle finger by a continuous blood pressure monitor (2300 Finapress, Ohmeda, Louisville, CO). All measurements were monitored and recorded continuously using an A-D converter with a programming software (LabView 5.0, National Instruments, Austin, TX) at a rate of 50 samples/s. Subjects were in sitting position throughout the study. Test hands were placed in a clear plastic chamber that was connected to a vacuum source and a pressure gauge. Both hands were positioned on an arm rest at heart level. After a stabilization period, a test with normal, ambient pressure (control) without the glove was performed to record baseline data. The chamber pressure was set from smaller to larger pressure differentials at the measuring site (ΔP), i.e., -50 mmHg without glove (ΔP= -50mmHg), -150 mmHg with glove (ΔP= +50mmHg), -100mmHg without glove (ΔP= -100mmHg), -100mmHg with glove (ΔP= +100mmHg), -50 mmHg with glove (ΔP= 150mmHg), and -150 mmHg without glove (ΔP= -150mmHg) in order to return to baselines conditions more rapidly and to reduce additive effects of repeated negative or positive pressures. In the condition without any glove, the skin of the hand was directly exposed to the negative pressures. This test

sequence also minimized any risk of injury to our volunteers. Right hands were exposed to each environmental pressure for five minutes, and the chamber was returned to normal atmospheric pressure until baseline values of blood flow were restored between each environmental pressure condition. For data normalization, baseline arterial blood pressure, pulse rate, and skin microvascular blood flow at the normal ambient pressure test were defined as 100%. Also, finger girth was set as zero percent just before each session and showed percentage changes from the normal ambient pressure condition. Skin temperature was measured in degrees Celsius and changes from that at normal ambient pressure condition were reported. Data points were generated by averaging the instantaneous signals over 10-second periods.

All data were expressed as means ± SE, and were analyzed by repeated measure ANOVA. If statistically significant effects were found, Fisher's post-hoc test was applied to compare between conditions. Significance was set at $p<0.05$.

RESULTS

External skin pressure generated by the glove against the hand was higher than the ambient pressure but somewhat variable depending upon site (Figure 2).

[Figure 2 Here]

At normal ambient pressure, the MCP glove effectively produces approximately 200 mmHg at the middle finger and on the hand dorsum (185.3±9.5, 187.0±23.1 mmHg, respectively). These pressures were maintained at -50, -100, -150 mmHg.

However, the pressure on the palm was significantly lower than that of middle finger and the dorsum (72.3±10.2mmHg at normal ambient pressure).

All subjects completed the entire protocol although they felt greater discomfort with higher levels of negative chamber pressure. We believe this discomfort was caused by the tighter seal around the wrist that was required during greater negative pressure. This discomfort was an artifact of the seal because it was located at the wrist only. It disappeared immediately after each exposure, and no adverse symptoms or signs (except redness of the skin) were observed after the entire protocol.

Without the glove, mean arterial blood pressure significantly increased with negative pressure (110.2±4.8, 120.0±3.8, 129.2±6.5% at -50, -100, -150 mmHg, respectively), compared to that of normal ambient pressure (range 71.2 - 100 mmHg) (Figure 3a). The blood pressure with the MCP glove was also increased (120.2±4.5, 125.4±8.1, 123.0±8.7%), but there were no significant differences between measurements with and without the MCP glove. Pulse rate did not change significantly (106.4±3.6, 103.7±4.9, 101.4±4.9 % without the glove vs. 105.7±7.3, 100.6±5.8, 104.0±6.7% with the glove at -50, -100, -150 mmHg , respectively), compared to that of normal ambient pressure (range 45.2 - 87.2 beats per minute) (Figure 3b).

Without the MCP glove, skin blood flow at the dorsum of the hand significantly increased at -50mmHg (2441.5±447.3%), and gradually decreased at -100mmHg(1680.1±362.6%) and -150mmHg (1578.8±204.9%), compared to that of normal ambient pressure (range 0.40 - 1.31 arbitrary units) (Figure 3c). With the

MCP glove, these large increases of skin microvascular flow were counteracted. Though the blood flow tended to increase with -50, -100 and -150mmHg (73.2±19.8, 168.6±40.2, 272.6±71.4%, respectively), they were not significantly different from those at normal ambient pressure. Due to the increase in blood flow without the MCP glove, the middle finger girth increased at -50, -100, -150 mmHg (1.0±0.5, 2.28±0.7, 3.1±0.7%, respectively). With the MCP glove at -50, -100 -150 mmHg, girth remained equal to that of normal ambient pressure (-0.24±0.15, 0.22±0.3, -0.02±0.4 %, respectively). In spite of increase in regional blood flow and finger girth, skin temperature significantly decreased with negative pressure (-4.9±0.43, -3.8±0.4, -2.8±0.6 °C at -50, -100, -150 mmHg, respectively). With the MCP glove, these decreases were also avoided and the temperature did not change significantly (0.4±0.7, -0.4±0.6, -0.6±0.4 °C at -50, -100, -150 mmHg, respectively), compared to that of normal ambient pressure (range 30.9-35.1°C).

[Figure 3 Here]

DISCUSSION

The prototype of the MCP glove generated pressures on the skin near 200 mmHg. The pressure on the middle finger showed 185.3±9.5 mmHg with the elastomeric material. The results indicate that the elastomeric material of the glove is capable of compressing cylindrical structures. This pressure did not change significantly at -50, -100, -150 mmHg. That means the pressure from the finger part of the MCP glove was proportional to the radius of the finger, and the material could maintain the

elasticity and tension over this range of negative pressures. Finger girth did not change due to stable MCP. Conversely, stable finger girth maintained MCP at the ambient pressures under study. The MCP glove requires an inflatable layer at the dorsum of the hand because flat or ellipsoidal surfaces do not as effectively receive surface compression from the elastic as round body parts (10). The inflatable layer in the glove maintained the surface pressure on the flat dorsum of the hand. The MCP glove can, therefore, exert pressures on the finger and dorsum of the hand to levels similar to current gas-pressurized EVA suit gloves. The current U.S. EVA suit, EMU, is pressurized with breathing oxygen at approximately 222mmHg (16, 18), or about 0.3 atmosphere. Even at this pressurization, present EVA suits are rigid, and thus severely restrict movement and performance. The Russian EVA suit (Orlan) is pressurized to 290 mmHg (5.6 psia) and has even greater mobility restrictions. If MCP is produced by a powerful elastic leotard, the mobility or flexibility should be improved. However, the pressure against the palm was significantly lower than that over the finger and the dorsum. The palm may be more resistant to negative pressure than the dorsum of the hand because the palm contains dense connective tissue septa in the superficial fascia that tether the skin to the deep fascia (3). However, to generate the same pressure as the current EVA glove, another resource will be needed for concave segments of the body.

In the present study, as a first step to develop MCP suits, we evaluated the local physiological effects of the MCP. With negative pressure, the skin blood flow significantly increased compared to that of normal ambient pressure. This result

contrasts with locally applied negative pressure (7, 13) or lower body negative pressure (LBNP) experiments (5, 9). The locally applied negative pressure generated by an air-filled plethysmograph with stiff walls or a sucking glass, decreases subcutaneous blood flow (7, 13). The decrease is caused by local sympathetic veno-arteriolar, arteriovenous reflex, which is probably due to an increase in vascular transmural pressure (7, 13) due to local pain (20) or reduced venous return due to local compression by the device (19). In the present study, local sympathetic nerves might be also activated, because arterial blood pressure on the finger was higher with negative pressure. However, because of a non-compressive bridge that prevents disturbance of the local circulation, microcirculatory blood flow was increased with negative pressure. Without the bridge, local venous drainage was disturbed. The wrist under the seal or negative pressure-exposed-hand experienced more pain, and blood flow at the dorsum of the hand was decreased as described in the other articles (our unpublished data). These differences in experimental condition, measuring site, or anatomical variations in subcutaneous interstitium might also cause the differences in results of the other articles. LBNP also decreased skin capillary blood flow in the foot (9) and forearm (5). With LBNP, the fluid shift unloads the carotid and cardiopulmonary baroreceptors, reflexively increasing sympathetic outflow (12), and thus constricting all arterioles. However, the blood shift is comparatively small in this study since only the right hand was exposed to negative pressure. Thus, baroreflex vasoconstriction responses are probably minor, because a small volume of

blood is shifted toward the hand. A rise in blood pressure without a significant change in pulse rate supports this hypothesis.

The MCP glove effectively compressed the skin and counteracted any increase in blood flow and finger girth. With the MCP glove on, blood flow did not change significantly although it tended to increase with negative pressure. With the MCP glove, the blood flow remained the same as the control value with the locally applied negative pressure up to -150mmHg. Middle finger girth also increased with negative pressure. As discussed above, arterial inflow increased, and venous blood volume also increased with negative pressure since the mercury strain gauge reflects local blood flow and venous volume repletion (11). Again, the MCP glove counteracted these changes and maintained the same girth compared to that of normal ambient pressure.

Skin temperature significantly decreased with negative pressure despite increased skin blood flow. Blood flow is the most important factor in skin temperature because the internal heat transportation is dependent on blood flow (14). However, skin temperature can change without changes in skin blood flow and vice-versa (15). A hypobaric environment and the air inflow from the bridge under the wrist seal lowers the skin temperature by enhanced evaporative heat transfer (4). Though air inflow was also observed during the MCP glove testing, the MCP glove significantly depressed these changes in temperature, and maintained control condition. Clothing might disturb the heat dissipation to the ambient environment (4).

In conclusion, the MCP glove effectively generated pressures equivalent to the current Shuttle EMU glove for EVA. Blood flow and finger girth were significantly increased during negative pressure exposures, while local skin temperature was decreased by negative pressure and air flow. These changes were effectively counteracted by the MCP glove.

ACKNOWLEDGEMENT

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REFERENCES (Incorporated herein by reference)

1. Adams JD, Dixon GA, Olson RM, Bassett BE, Fitzpatrick EL. Preventing of bends during space Shuttle EVA's using stage decompression. In: Preprints of the 1981 Aerospace Medical Association Meeting: Washington, DC: Aerospace Medical Association, 1981; 55.

2. Annis JF, Webb P. Development of a Space Activity Suit. NASA CR-1892 1971; 1-134.

3. Bojsen-Møller F, Scmidt L. The palmar aponeurosis and the central space of the hand. J Anat. 1974; 117: 55-68

4. Chang SK, Santee WR. Clothing insulation in a hypobaric environment. Aviat. Space Environ. Med. 1996; 67: 827-834.

5. Essandoh LK, Houston DS, Vanhoutte PM, Shepherd JT. Differential effects of lower body negative pressure on forearm and calf blood flow. J. Appl. Physiol. 1986; 61: 994-998.

6. Hargens AR, McClure AG, Skyhar MJ, et al. Local compression patterns beneath pneumatic tourniquets applied to arms and thighs of human cadavera. J. Ortho. Res. 1987; 5: 247-252.

7. Henriksen O, Sejrsen P. Local reflex in microcirculation in human cutaneous tissue. Acta Physiol. Scan. 1976; 98: 227-231.

8. Hills BA. Compatible atmosphere for a space suit, space station, and shuttle based on physiological principles. Aviat. Space Environ. Med. 1985; 56:1052-1058.

9. Jacobsen TN, Nielsen HV, Kassis E, Antorp, Ø. Subcutaneous and skeletal muscle vascular responses in human limbs to lower body negative pressure. Acta. Physiol. Scand. 1992; 144: 247-252.

10. Megyesy EF. External pressure. In: Megyesy EF ed. Pressure vessel handbook. 4th ed. Tulsa, OK: Pressure handbook publishing, inc, 1977; 29-43.

11. Peirce EC, Premus G, Martinelli G, Schanzer H. Foot blood flow measurements improve venous plethysmographic studies. Surgery 1987; 101: 422-429.

12. Rea RF, Wallin BG. Sympathetic nerve activity in arm and leg muscles during lower body negative pressure in humans. J. Appl. Physiol. 1989; 66: 2778-2781.

13. Skagen K, Henriksen O. Chages in subcutaneous blood flow during locally applied negative pressure to the skin. Acta Physiol. Scan. 1983; 117: 411-414.

14. Sparks HV. Skin and muscle. In: Johnson PC ed. Peripheral circulation. New York: John Wiley & Sons, 1978; 193-230.

15. Thauer R. Circulatory adjustments to climatic requirements. In: Hamilton WF, Dow P ed. Handbook of Physiology vol. 3, sec 2. Washington DC, American Physiological Society. 1965; 1921-1961.

16. Vann RD, Torrebueno JR. A theoretical method for selecting space craft and space suit atmospheres. Aviat. Space Environ. Med. 1984; 55: 1097-1102.

17. Webb P. The space activity suit: An elastic leotard for extravehicular activity. Aerospace Med 1968; 38: 376-383.

18. Webb P, Annis JF. The principle of the space suit. NASA CR-973, 1967; 1-29.

19. Xakellis GC, Frantz, RA, Arteaga M, Meletiou, S. A comparison of changes in the transcutaneous oxygen tension and capillary blood flow in the skin with increasing compressive weights. Am. J. Physic. Med. Rehab. 1991; 70: 172-177.

20. Zhang T, Huang C, Johns EJ. Neural regulation of kidney function by the somatosensory system in normotensive and hypertensive rats. Am. J. Physiol. 1997; 273: R1749-R1757.

21. Apparatus promoting flow of a body fluid in a human limb. Patent 4,370,975.

22. Circulation enhancing apparatus. Patents 5,458,562, and 5,000,164.

23. Drug-free method for treatment of the scalp for therapeutic purposes, . Patent 5,228,431.

24. Use of hallow hypobaric chambers on body parts for increasing blood flow, reducing pressure and decreasing pain. Patent 5,425,742.

25. Method and apparatus for augmenting blood circulation. Patent 4,738,249.

26. Apparatus and method for core body warming of mammals experiencing hypothermia. Patent 5,683,438.

27. Therapeutic method for treating ulcers. Patent 6,135,116.

28. Bird, A.D., et al. Effect of hyperbaric oxygen on limp circulation. Lancet 1 :355-356, 1965.

29. Haapaniem, T. Hyperbaric oxygen treatment reduces ischemic-induced skeletal muscle injury. Plastic Reconstructive Surgery 97: 602-607, 1996.

30. Ubbink, D.T., et al. Effects of vacuum compression therapy on skin microcirculation in patients suffering from lower limb ischaemia. VASA 29: 53-57, 2000.

31. Skagen, K., et al. Changes in subcutaneous blood flow during locally applied negative pressure to the skin. Acta Physiol Scand 117: 411-414, 1983.

32. Muha, J. Local wound care in diabetic foot complications. Postgraduate Medicine 106: 97-102, 1999.

LEGENDS

Figure 1

The force-sensing array placed on the hand. The array was placed along the palm, the middle finger and the dorsum of the hand.

Figure 2

The pressure generated by the mechanical counter pressure glove on the palm, the middle finger and the dorsum of the right hand. *$p<0.0001$, compared to the middle finger value. †$p<0.0001$, compared to the dorsum value.

Figure 3

Physiological parameters with and without the mechanical counter pressure (MCP) glove in the chamber. Open circle shows the value with naked hand. Closed circle shows the values with the MCP glove.

a. Relative changes in arterial blood pressure. The value at the normal ambient pressure was defined as 100% (control). *$p<0.05$, compared to control value.
b. Relative changes in pulse rate. The value at the normal ambient pressure was defined as 100% (control).
c. Relative changes in skin capillary blood flow at the dorsum of the hand. The value at the normal ambient pressure was defined as 100% (control). *$p<0.05$, compared to control value. †$p= 0.0006$

d. Differnces in middle finger girth. The value just before each session was defined as 0%. *$p<0.05$, compared to control value. †$p=0.0013$

e. Skin temperature differences at the dorsum of the hand. The value shows the difference from that of normal ambient (control). *$p<0.05$, compared to control value. †$p=0.0001$.

simulates the acute increase in intra-ocular pressure that occurs in microgravity. The 6°HDT position, a commonly used method of simulating physiological changes secondary to microgravity exposure, did not produce the rise in intra-ocular pressure that has been found during space missions.

[156]
POSITIVE AND NEGATIVE COUNTERPRESSURE DIFFERENTIALS DECREASE AND INCREASE SKIN MICROVASCULAR FLOW IN THE HAND

J. Tanaka[1], J. Waldie[1], G. Steinbach[1], P. Webb[2], D. Tourbier[3], J. Knudsen[3], C. Jarvis[4] and A. Hargens[1]
[1]*Department of Orthopaedics, University of California, San Diego, CA;* [2]*Webb Associates;* [3]*Honeywell;* [4]*Clemson Apparel Research*

Introduction: Current space suits are bulky, rigid, gas-pressurized shells that protect the astronaut from the vacuum of space. A tight elastic garment, or mechanical counter pressure (MCP) suit, that generates pressure by compression may be an economical, safe and more flexible alternative. In the present study, we investigated local microcirculatory effects produced by extreme overpressure or underpressure exposures on the hand to help develop a MCP glove. Methods: The right hand of seven normal volunteers was subjected to 150 mmHg overpressure and underpressure. A laser Doppler blood perfusion probe and thermistor were placed on the dorsum of the hand. A vacuum chamber was used for the underpressure test of the exposed hand, while a MCP glove was donned to provide overpressure. After a stabilization period, all data were measured continuously for 5 minutes in each condition. Results: During 150 mmHg overpressure, skin microvascular flow decreased 42±7% (mean±SE) compared to normal, ambient pressure conditions ($p=0.0018$). During 150 mmHg underpressure, skin microvascular flow increased by 533±163% ($p=0.0049$). Skin temperature did not change significantly for either underpressure or overpressure tests. Discussion: During overpressure, skin blood flow decreased because arterial blood inflow and capillary perfusion were occluded. The distention of skin tissue and capillaries and some local effects of somatosensory stimulation probably increase skin microvascular flow during underpressure. Skin temperature did not change due to the short duration of the tests. The relatively great alterations of microvascular flow suggest that a MCP glove should supply skin surface pressure differentials of less than 150 mmHg. (NASA grant NAG9-1916 and Honeywell contract S00001263)

Tuesday, May 8 *2:00PM*

PANEL: Refractive Surgery Update for Aviators, Pt. 1: Navy Session

[157]
PANEL SUMMARY: REFRACTIVE SURGERY UPDATE FOR AVIATORS-- JOINT OVERVIEW PANEL AND NAVY SESSION

D. Holland[1], K. Belland[2] and C. Barker[3]
[1]*Naval Air Warfare Center, Lexington Park, MD;* [2]*IAMFSP, Fallon, NV;* [3]*US NAVY BUMED-Code 23, Washington, DC*

Discussion: This combined two-session panel has two components-- a NAVY panel of six papers that highlights the work going on at Naval Medical Center, San Diego, and a joint-service overview presentation and discussion panel. Following the NAVY session which delves into the various aspects of PRK for Naval Aviation-- the joint overview session contains brief papers by Army (C. VandePol), USN (S. Schallhorn), USAF (D. Ivan), and academic (I. Zimmer-Galler) researchers. After these papers are presented, a discussion panel is convened at the end of the second 90 min session which adds new individuals working with, or for, other governmental agencies including NASA (K. Manuel), the US Army (M. Lattimore), and the FAA (V. Nakagawara). CAPT C. Barker, USN, will moderate the discussion portion of this session.

[158]
UPDATE ON PHOTOREFRACTIVE KERATECTOMY IN NAVAL AVIATION

D. Tanzer[1], S. Schallhorn[1] and M. Brown[1]
Naval Medical Center, San Diego, CA

Purpose: To provide an update on the "Retention of Naval Aviator" PRK protocol. Methods: To date, 164 aviators have been enrolled in the retention study: 14% pilots, 69% NFO/WSO's and 17% other class 2 aviators. Community enrollment to date is as follows: fighter/attack - 40%, electronic warfare - 25%, helicopter - 8%, anti-submarine warfare - 18%, other - 7%. There are two laser centers (San Diego and Portsmouth) and over 15 follow up sites employed in the study. Results: Average preop mean spherical equivalent (MSE) refraction was -2.80 diopters (D). At 4 weeks postop (the soonest an aviator can be found medically cleared to fly following surgery), average MSE was +0.09 D. Average uncorrected visual acuity (UCVA) before surgery was 20/200, and by the final exam UCVA averaged 20/16. 87% of aviators had UCVA of 20/20 or better by 4 weeks following PRK and were eligible to fly without corrective lenses. By 2 months following surgery, 92% of aviators had 20/20 or better UCVA. By 3 months post op, 23% had 20/10 UCVA, 32% were 20/12, 28% were 20/16 and 6% were 20/20. 73% of enrolled aviators were medically cleared to fly by 4 weeks following surgery, 98% were cleared by 8 weeks and 100% of enrolled aviators met return to flight criteria by 12 weeks following surgery. By the end of FY00, a total of 294 flight hours had been logged by post-PRK aviators, including 57 hours flown at night. A total of 75 landings had been carried out, including 30 night landings, 60 field carrier landing practice landings and 6 carrier arrested landings (2 at night). Conclusions: To date, the results of the "Retention of Naval Aviator" protocol have been outstanding. However, there have been complications, including 2% the study population who did not meet return to flight criteria until 12 weeks following surgery and one aviator who required a medical evacuation from an aircraft carrier at sea for a corneal erosion following PRK. The protocol will proceed and the debate will continue as to the appropriateness of refractive surgery in aviators. Thus far, the results look promising.

[159]
FLIGHT PERFORMANCE AND VISION STANDARDS IN STUDENT NAVAL AVIATORS AFTER PRK

M. Brown[1], S. Schallhorn[1], D. Tanzer[1] and J. Grimson[1]
[1]*Naval Medical Center San Diego, CA*

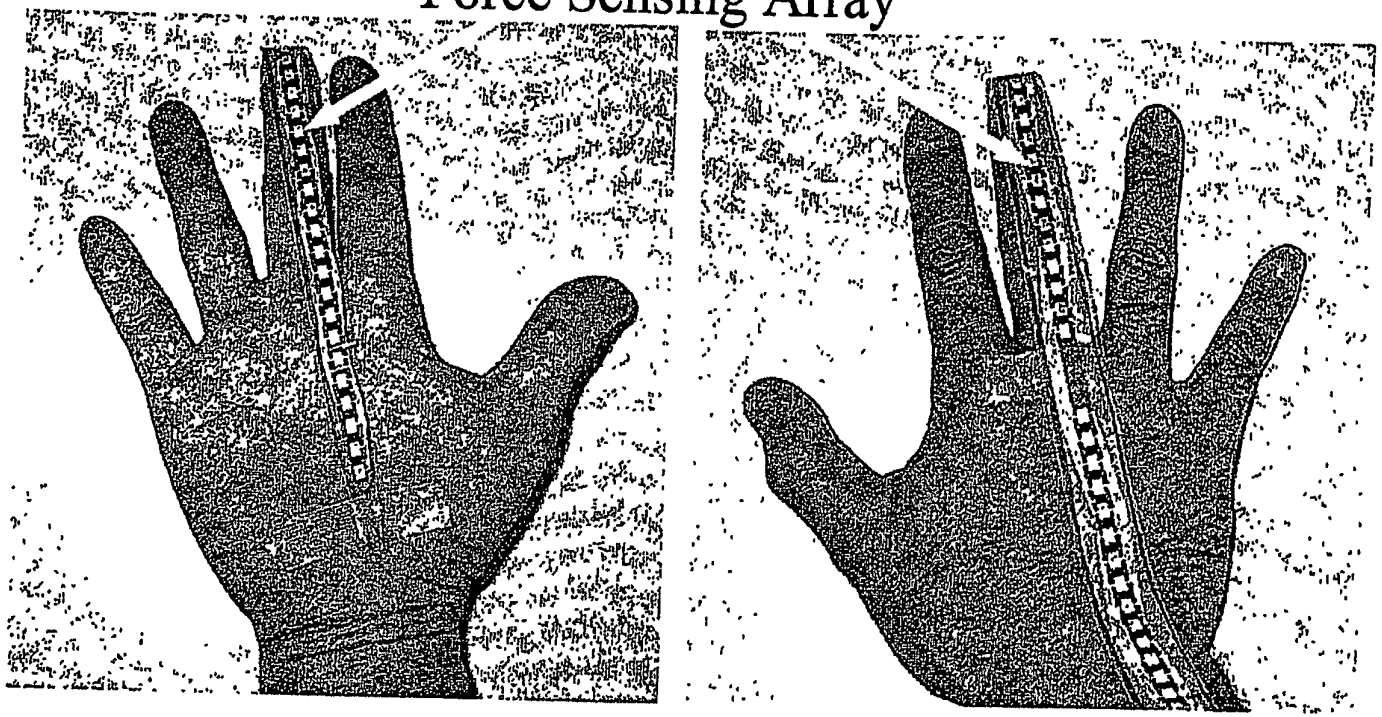
Purpose: To prospectively evaluate flight performance in Student Naval Aviators (SNA) and Student Naval Flight Officers (SNFO) who have previously undergone Photorefractive Keratectomy (PRK), and to compare their performance to student controls. To evaluate the role of refractive surgery in the Naval aviation accessioning process. Methods: 250 SNAs and 250 SNFOs who have had PRK will be enrolled. Subjects must meet all inclusion and exclusion criteria for the study, and with the exception of a history of PRK must be otherwise physically qualified (PQ) and aeronautically adaptable (AA) for SNA or SNFO. Accessioning sources include the United States Naval Academy (USNA), NROTC, direct accessions and active duty personnel. PRK will not be performed by the Navy as part of the study, however a group of USNA midshipmen will be offered PRK each year with the intent of increasing the qualified applicant pool for Naval aviation training. Flight performance will be evaluated using standardized grading methods for individual training elements and overall performance in each phase of training. Other performance measures will include number of hours to complete training, attrition and mishap rates. Results: Standardized performance measures will enable direct comparison of flight performance in students who have had PRK against those who have not. Conclusions: Conclusions to be drawn from the study include safety and applicability of PRK in Naval aviation both as a means to reduce or eliminate dependence on eyeglasses or contact lenses, and as a mechanism to increase the pool of qualified applicants for Naval aviation training. Refractive surgery technology could potentially facilitate a shift in the pilot selection process, which will enable selection from a larger applicant pool based upon the most qualified candidates, not just the candidates with the best vision.

[160]
FROM PRE-OP TO CARRIER QUALS: A HORNET PILOT'S EXPERIENCE WITH PRK

M. Brown[1], T. David[1], S. Schallhorn[1] and J. Grimson[1]
[1]*Naval Medical Center San Diego, CA*

Purpose: A case report of a Navy F/A-18 pilot who underwent photorefractive keratectomy (PRK) for the correction of myopia. Report will include clinical data, aeromedical issues, and the pilot's perspective on PRK in Naval aviation with emphasis on carrier-based flight operations. Methods: The patient is a 36 year old male F/A-18 pilot with myopia in both eyes. Although contact lenses provided adequate vision for most tasks, they consistently failed to provide the visual resolution required for carrier-based flight operations. So despite the numerous limitations and problems associated with eyeglasses in the tactical jet environment, glasses were his preferred method of vision.

Force Sensing Array



Palm Side

Dorsum Side

FIG. 1

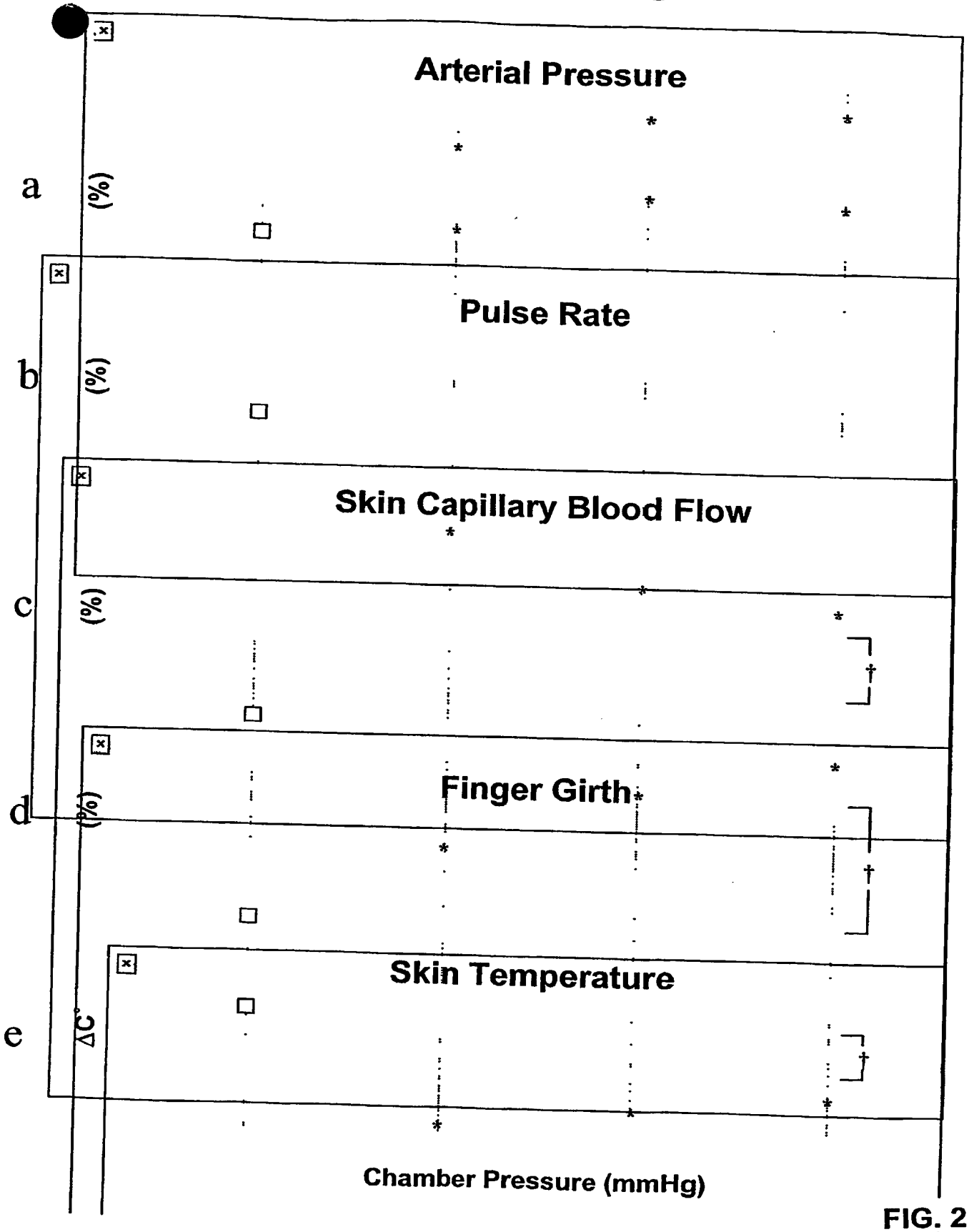

Arterial Pressure
a
(%)
Pulse Rate
b
(%)
Skin Capillary Blood Flow
c
(%)
Finger Girth
d
(%)
Skin Temperature
e
ΔC°
Chamber Pressure (mmHg)

FIG. 2

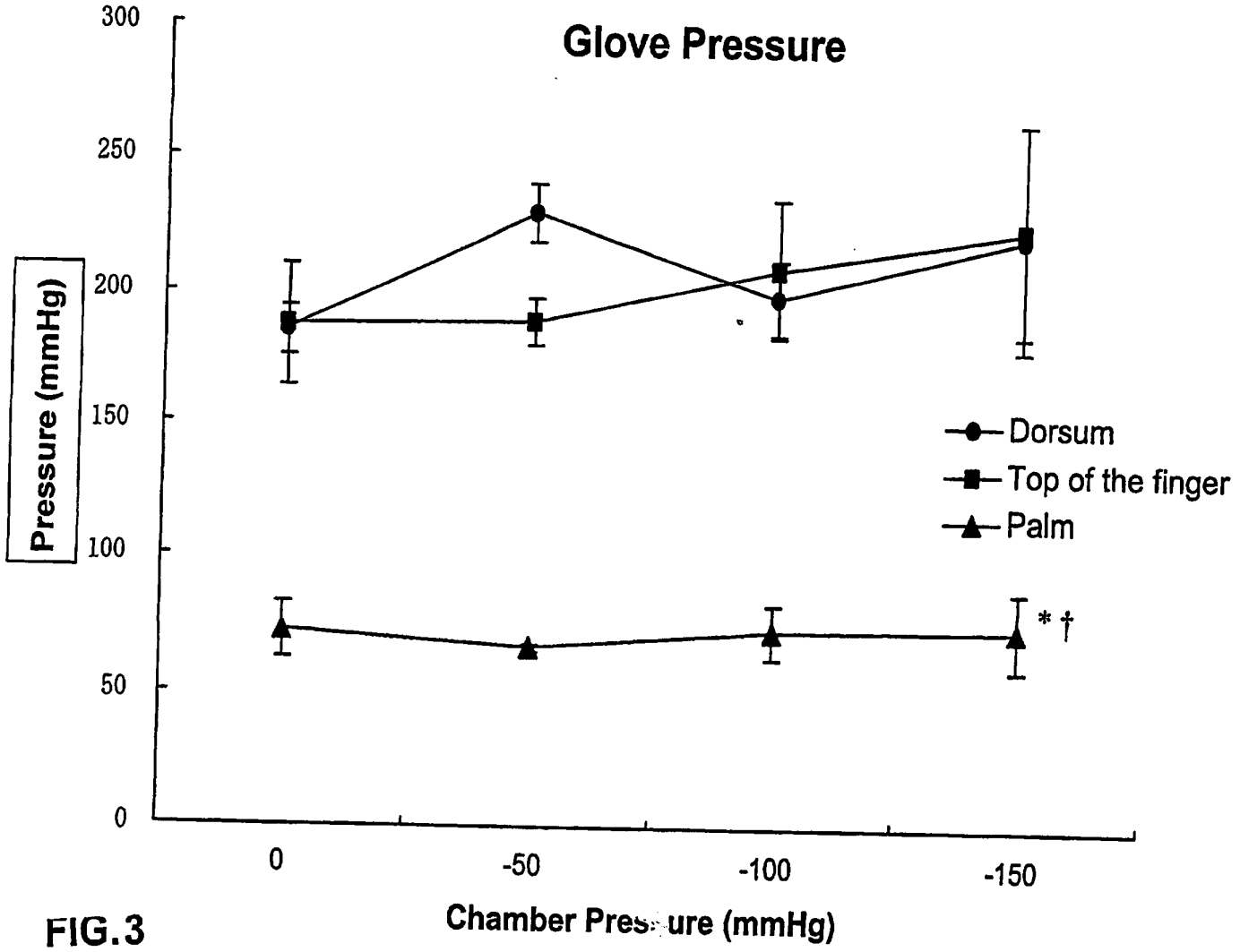

Glove Pressure
Pressure (mmHg)
300
250
200
150
100
50
0
0
-50
-100
-150
Chamber Pressure (mmHg)
Dorsum
Top of the finger
Palm
* †

FIG.3

NASA Studies in early 1990s

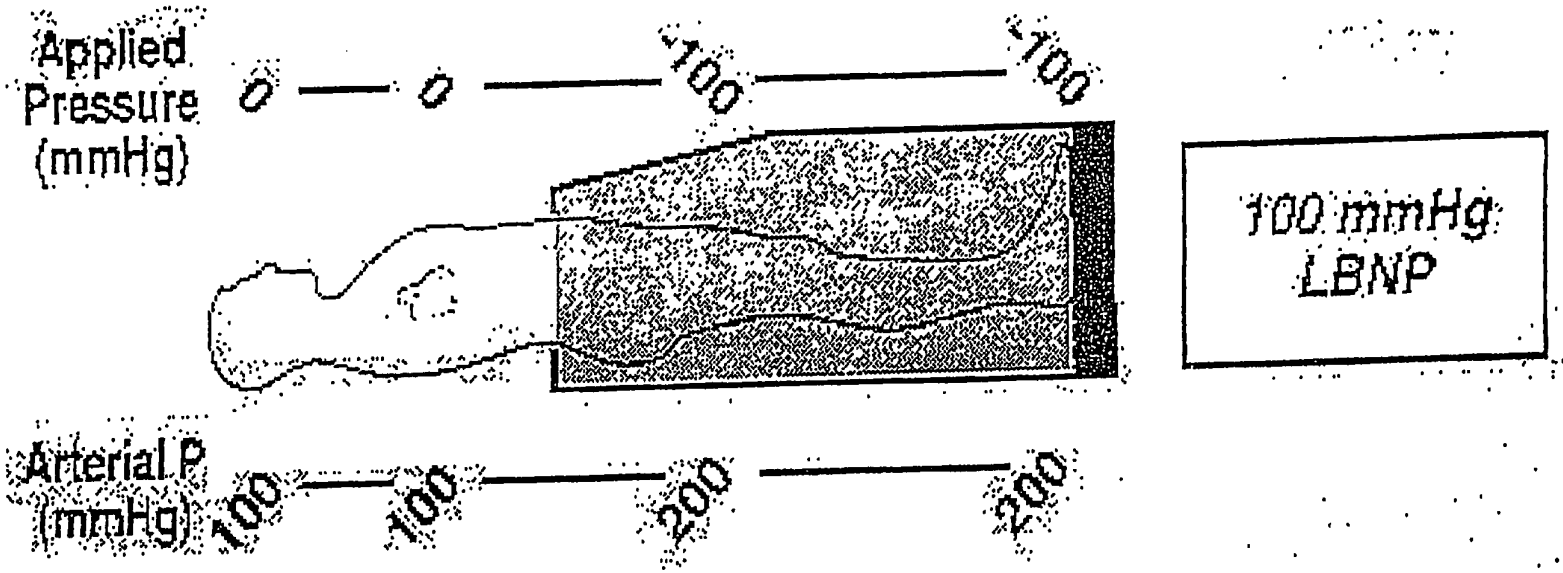


Fig. 4

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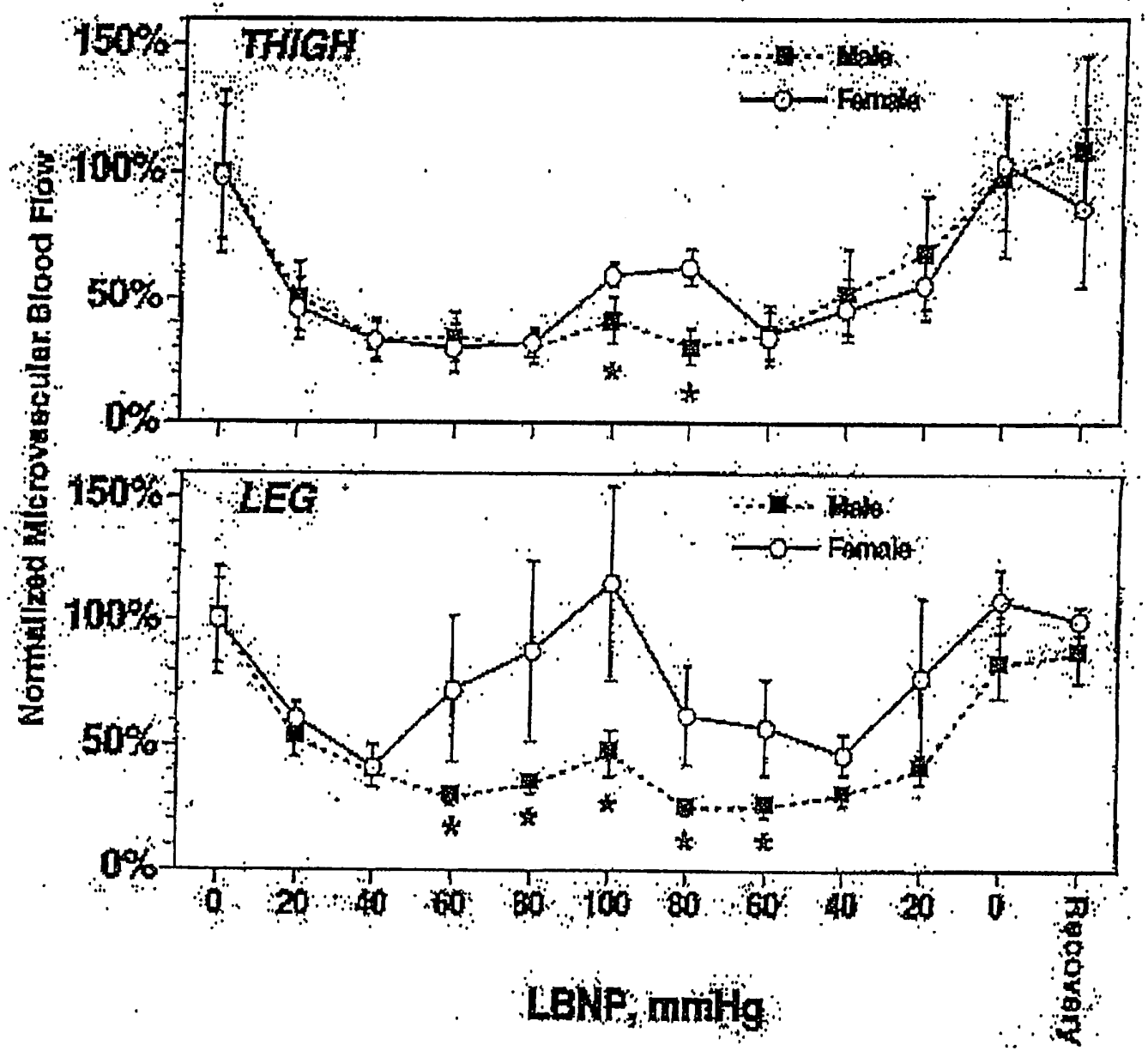
THIGH
LEG
Male
Female
150%
100%
50%
0%
Normalized Microvascular Blood Flow
0
20
40
60
80
100
80
60
40
20
0
LBNP, mmHg
RECOVERY

Fig. 5

CONFIDENTIAL

Fig. 6

New Technology (Loose Seal)

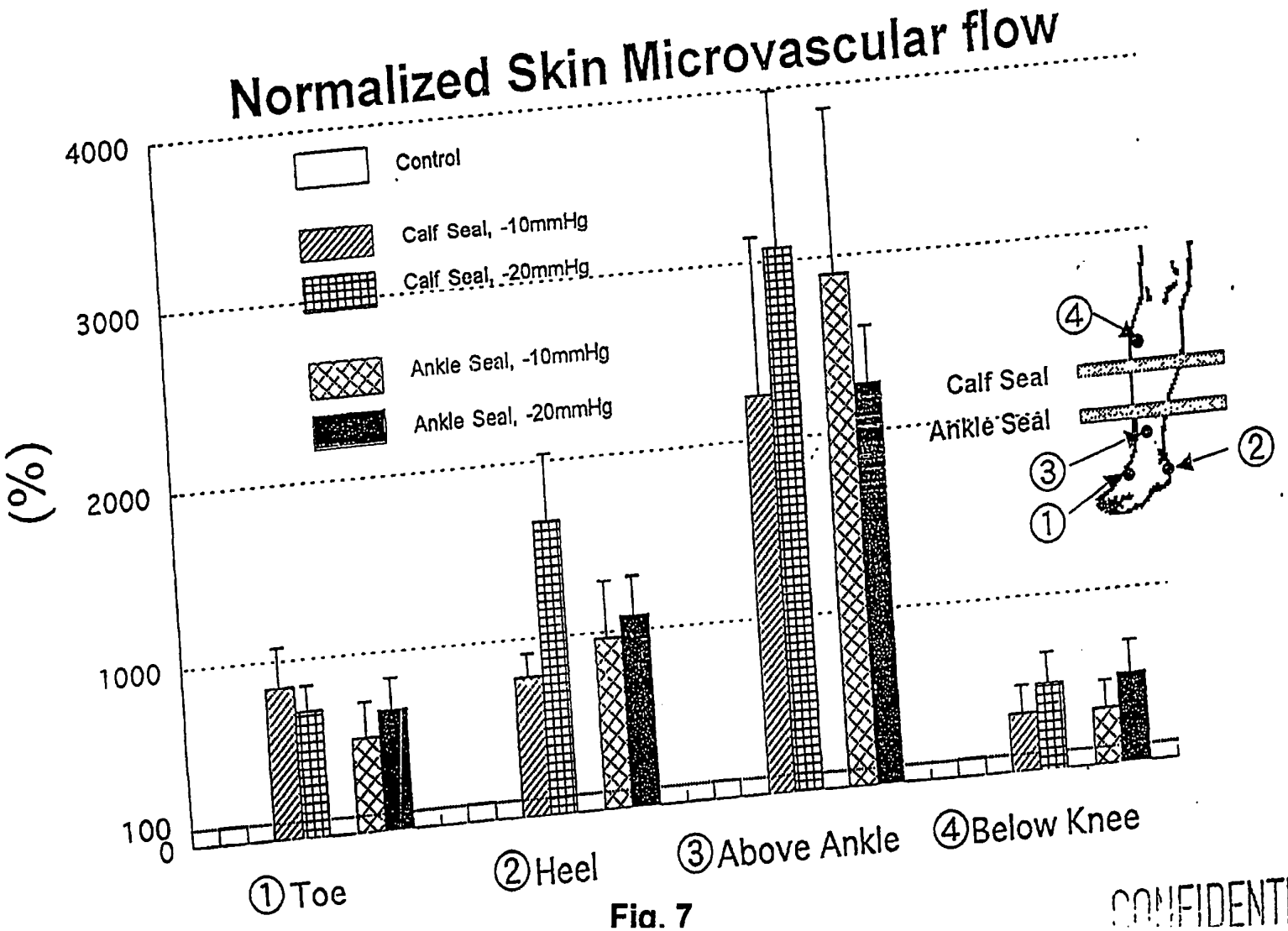

Fig. 7

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Old Technology (Tight Seal)

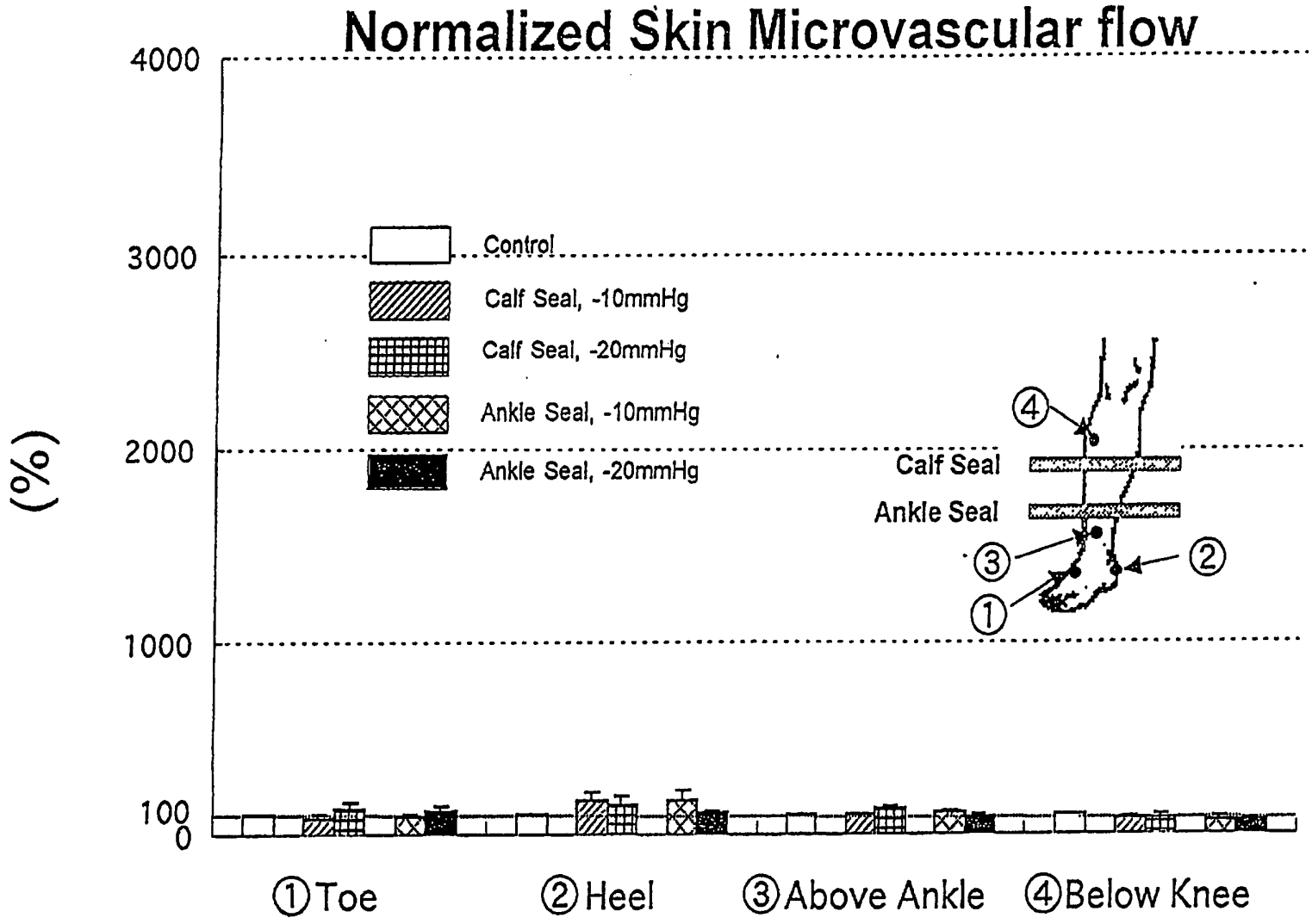

Fig. 8

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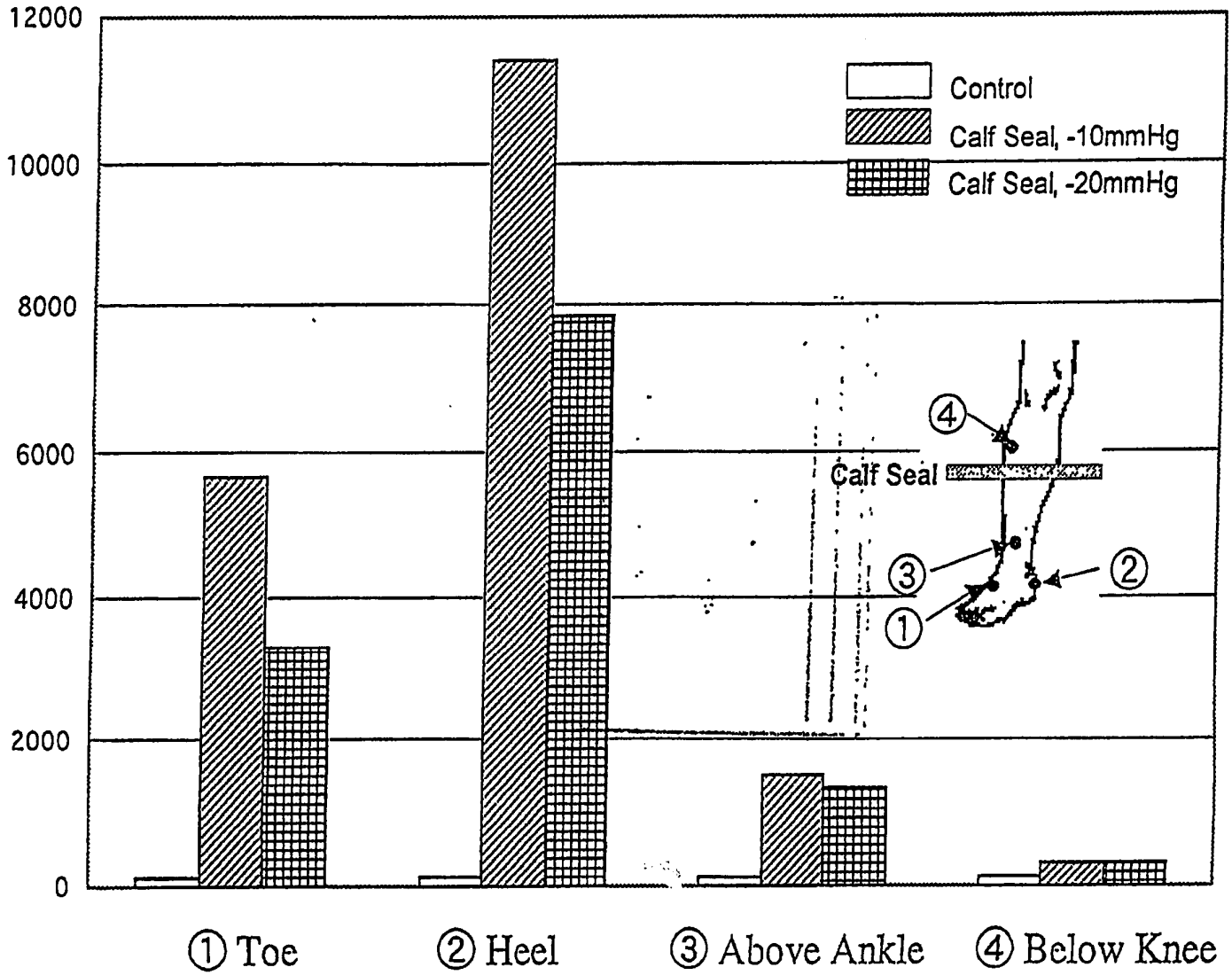
Normalized Skin Microvascular flow
(DM patient)



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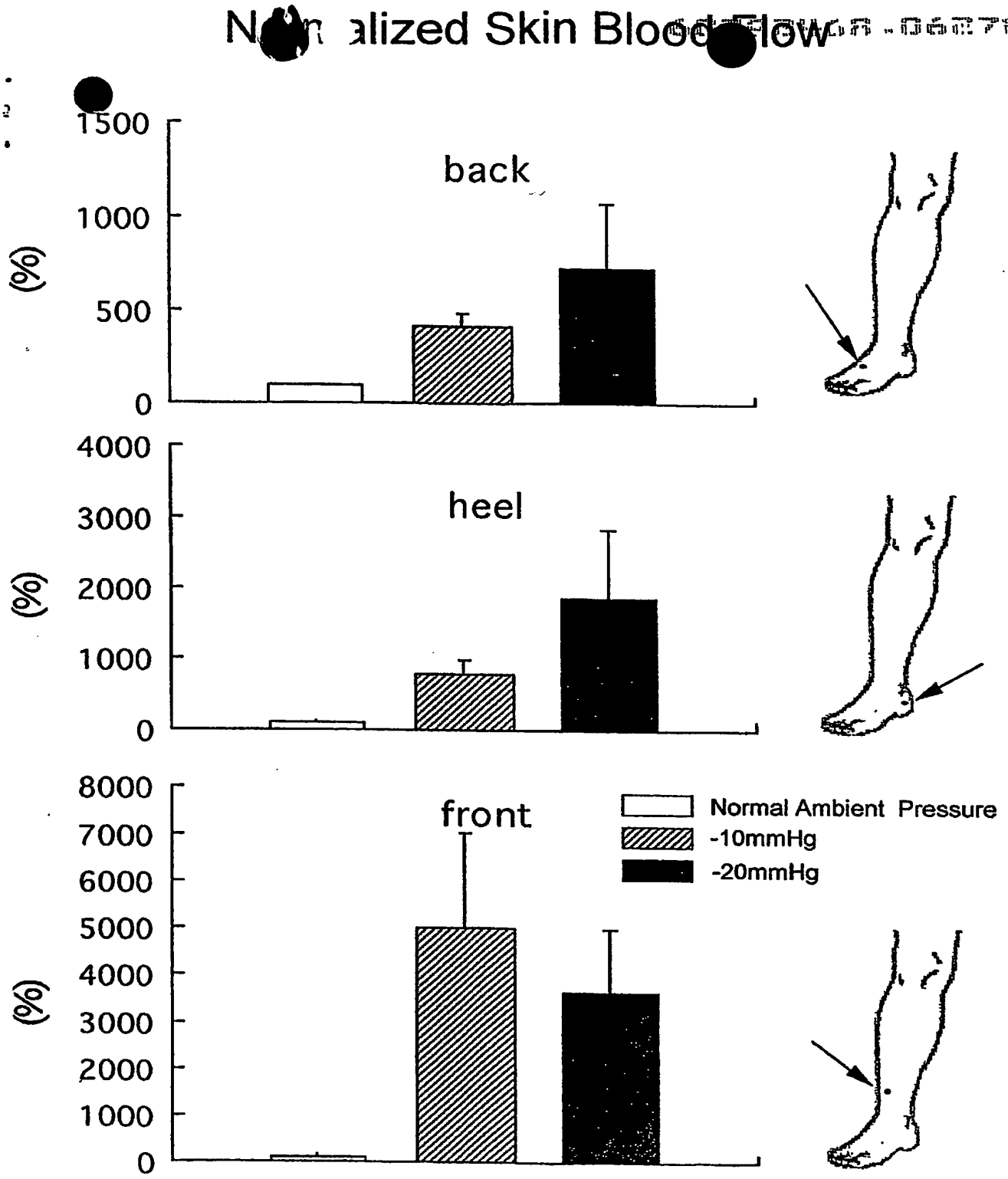
Normalized Skin Blood Flow
back
heel
front
(%)
1500
1000
500
0
4000
3000
2000
1000
0
8000
7000
6000
5000
4000
3000
2000
1000
0
Normal Ambient Pressure
-10mmHg
-20mmHg

Fig. 10

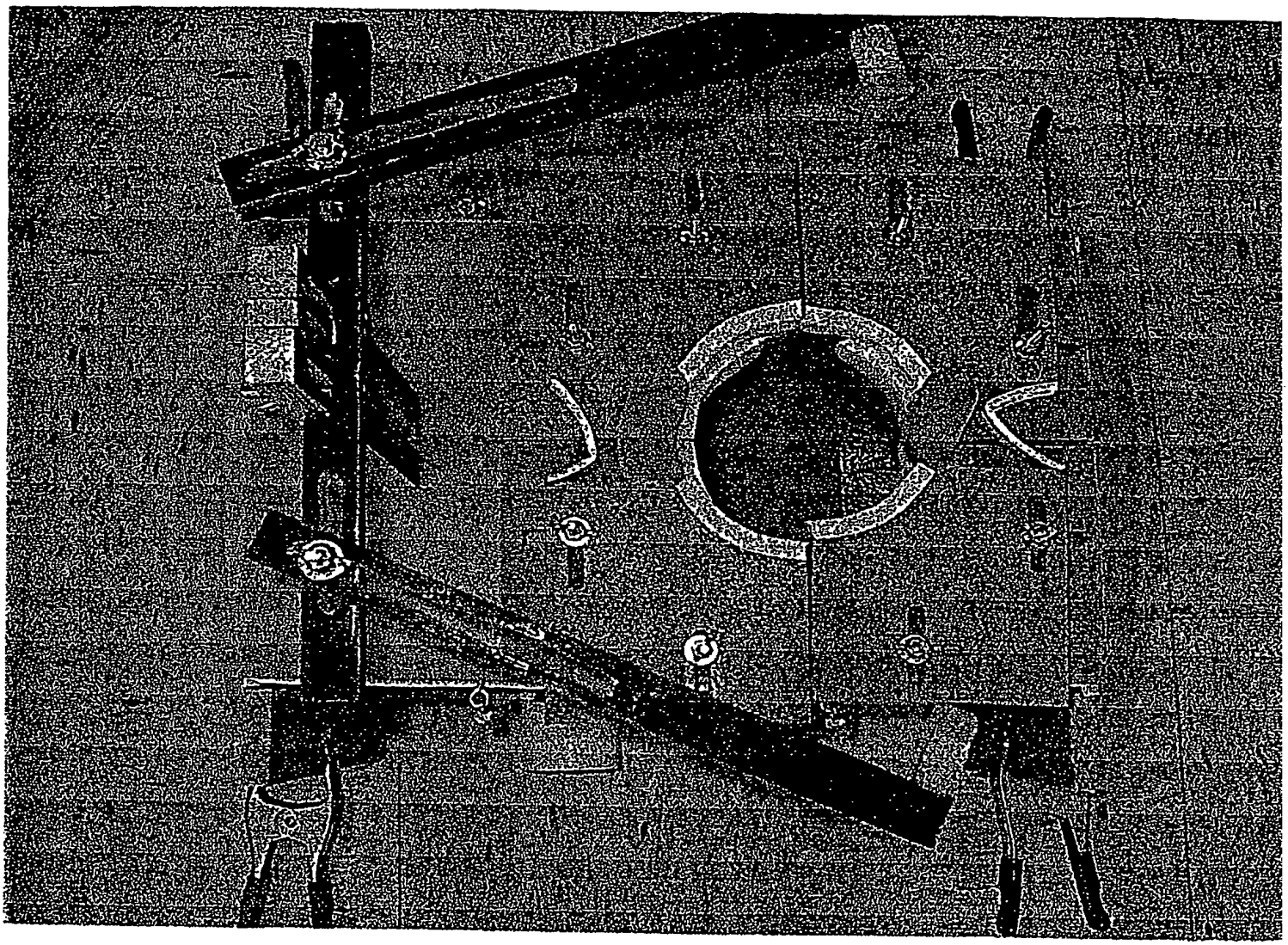

Fig. 11

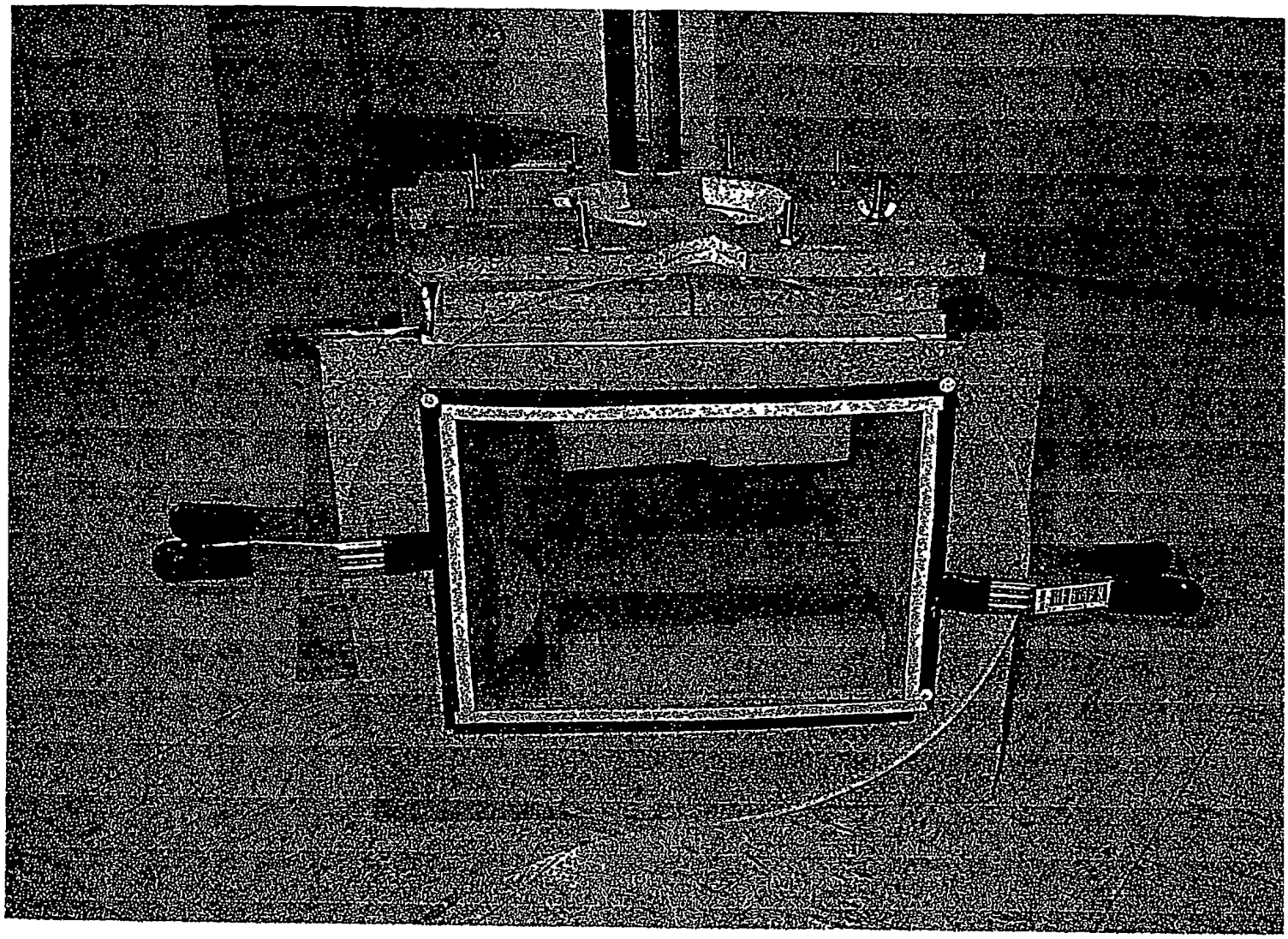

Fig. 12

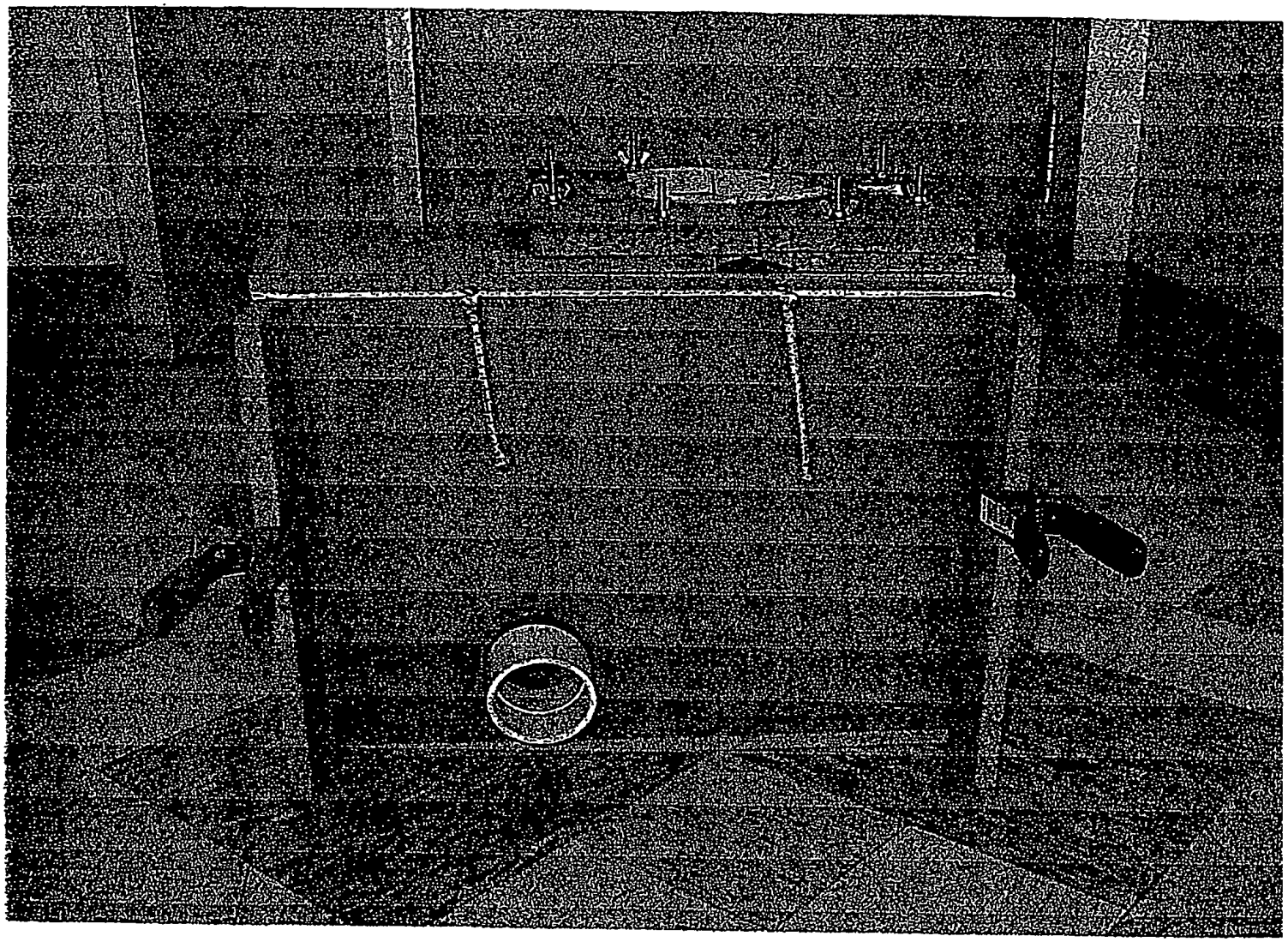

Fig. 13

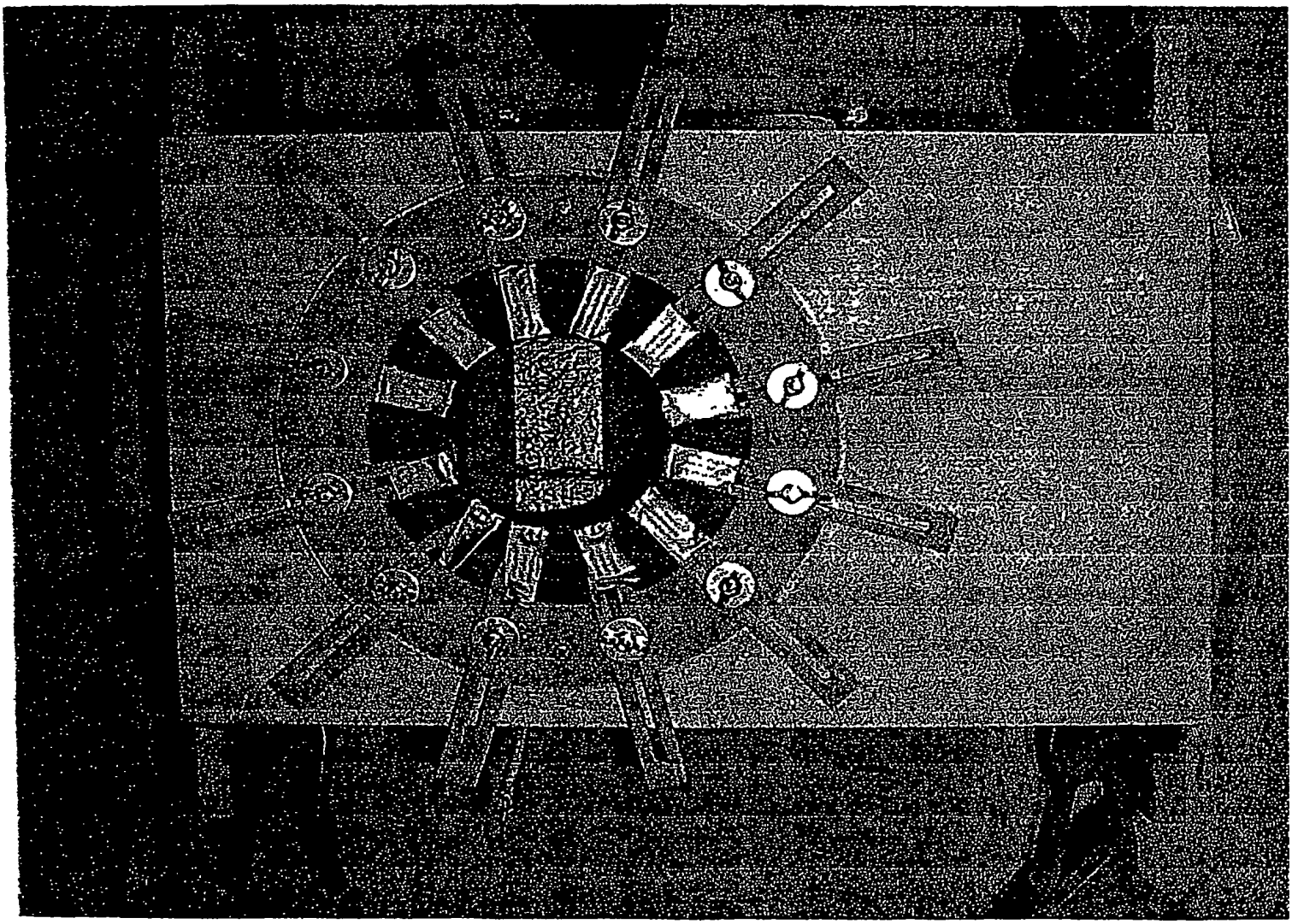

Fig. 14

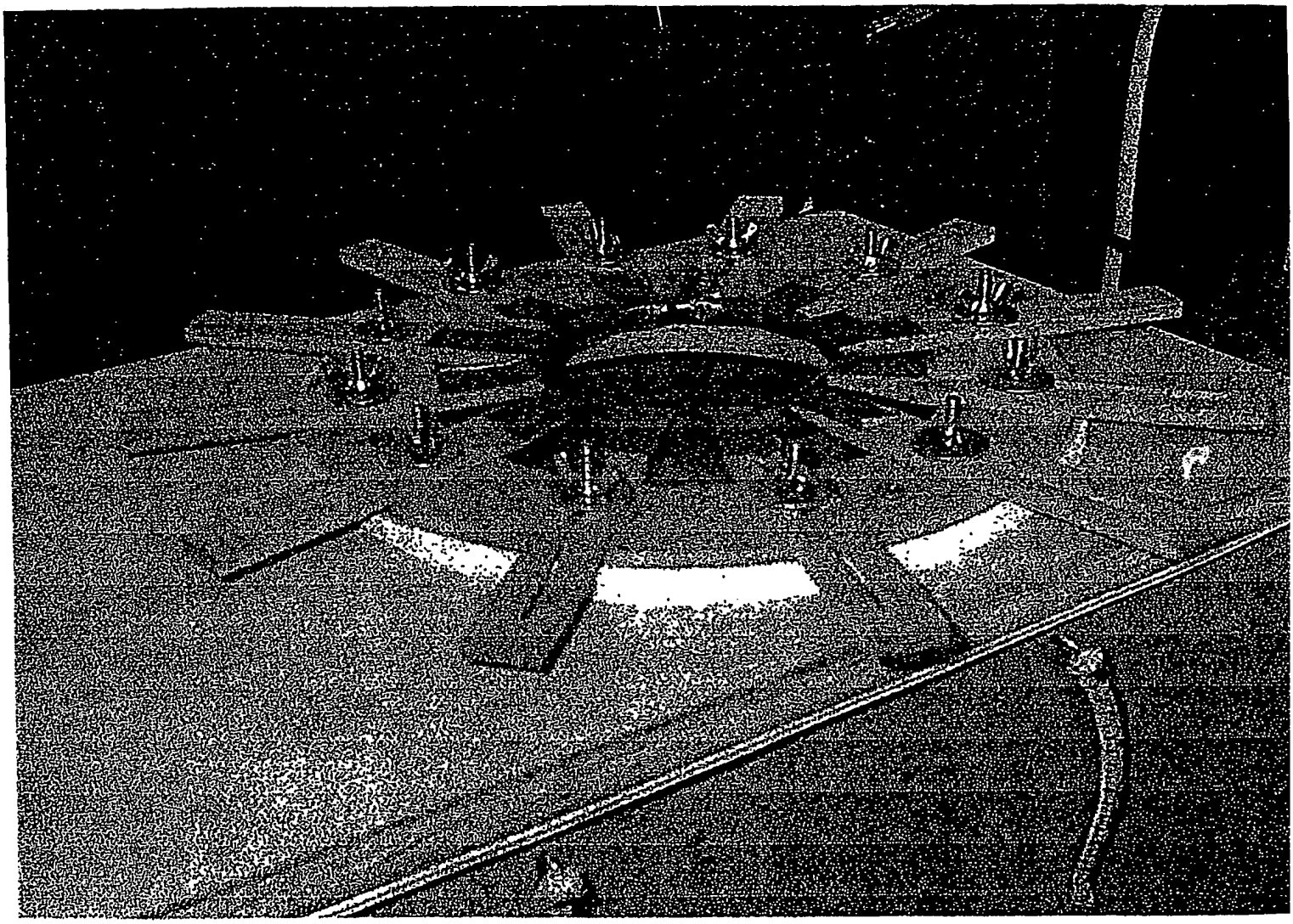

Fig. 15

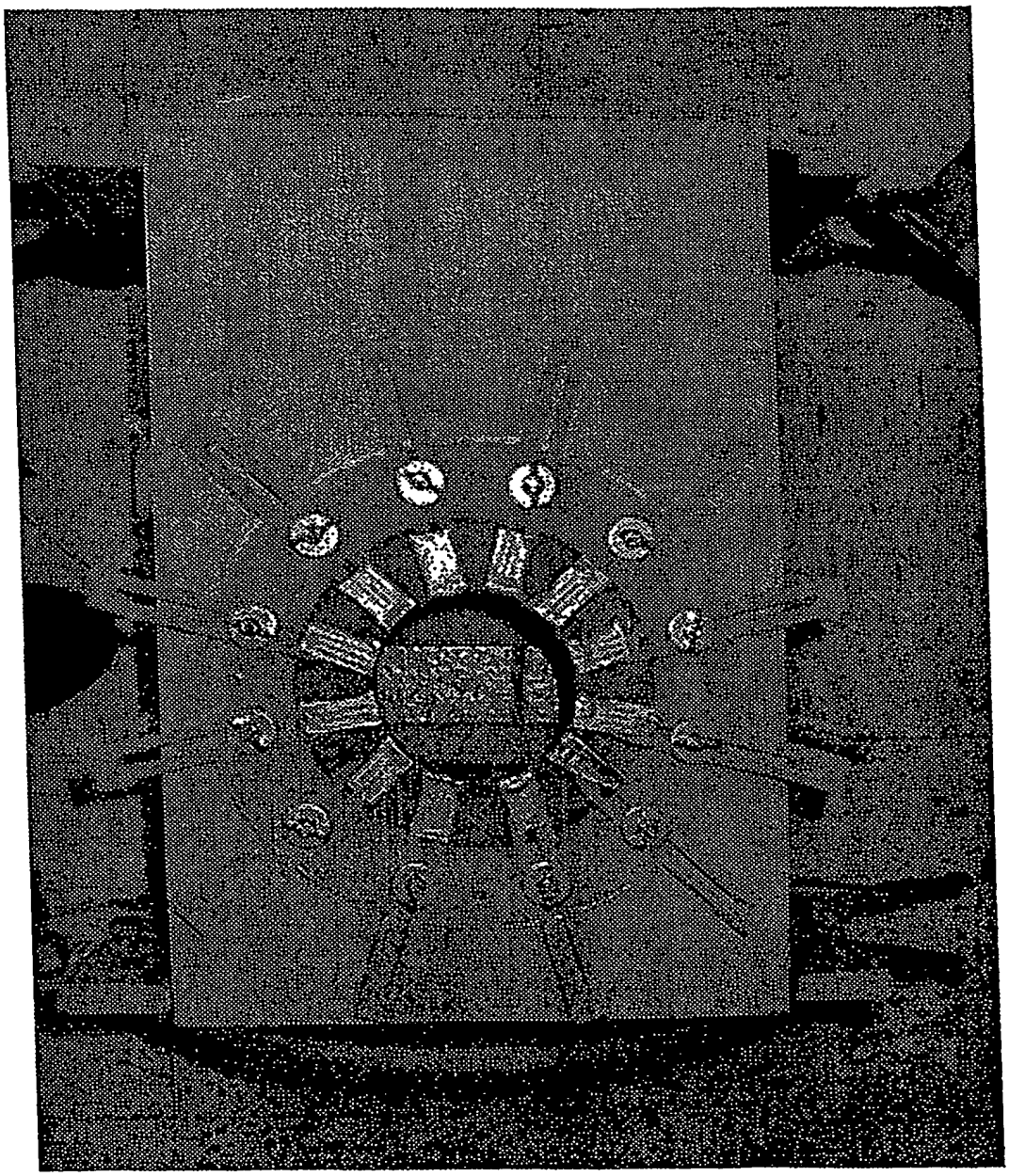

Fig. 16

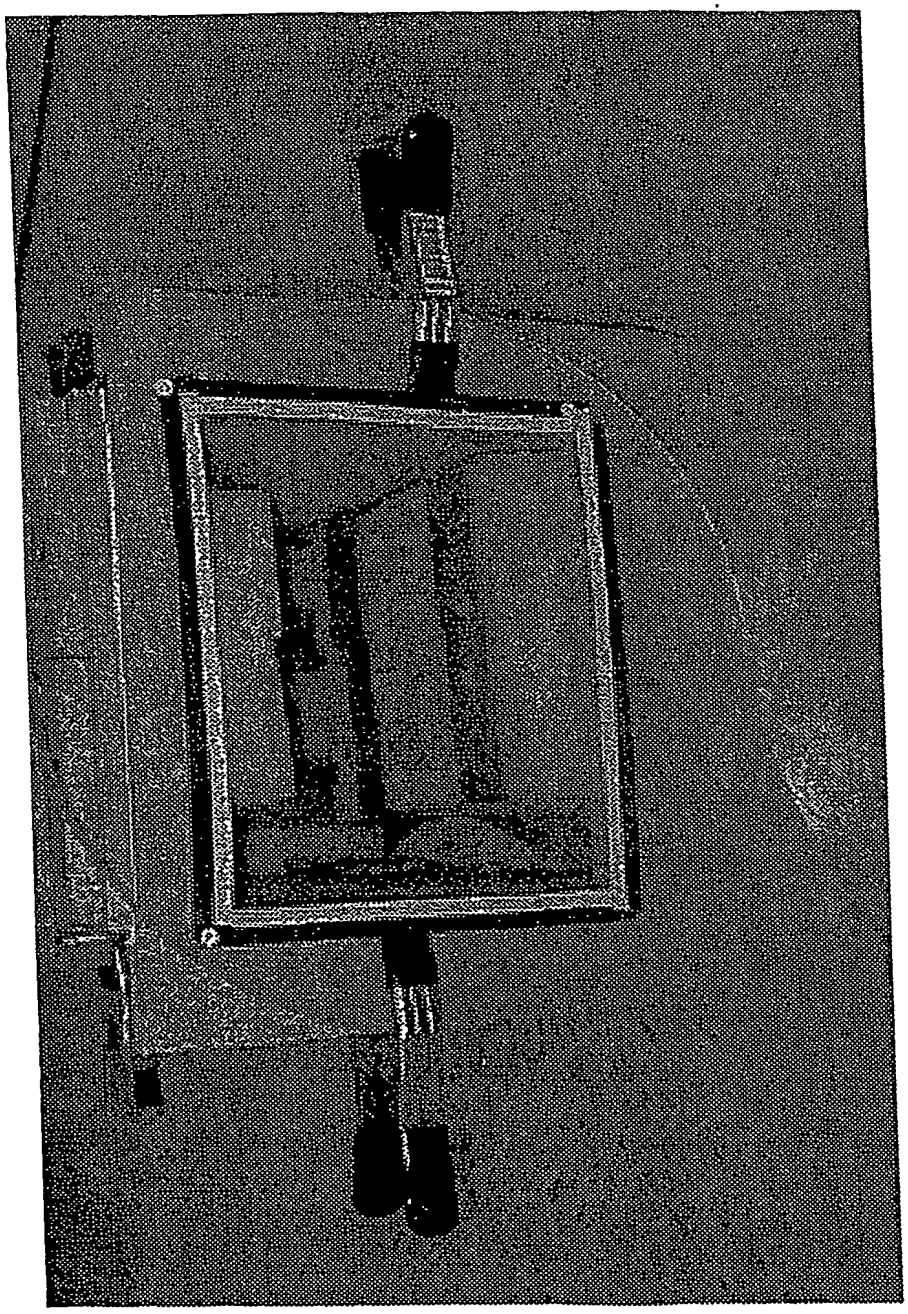

Fig. 17

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